CLAIMS

We claim:

1. A formulation for treating a patient for a neoplasm by inhalation comprising: an effective amount of a vesicant and a pharmaceutically acceptable carrier, wherein said vesicant does not exhibit substantial pulmonary toxicity.

2. The formulation according to Claim 1, wherein said vesicant comprises a moderate vesicant.

3. The formulation according to Claim 1, wherein said vesicant comprises paclitaxel and carboplatin.

4. The formulation according to Claim 1, wherein said moderate vesicant comprises: a non-encapsulated anticancer drug, wherein when 0.2 ml of said drug is injected intradermally to rats, at the clinical concentration for parenteral use in humans:

(a) a lesion results that is at least 20 mm^2 in area fourteen days after said intradermal injection; and

(b) at least 50% of the tested rats have this size of lesion.

5. The formulation according to Claim 1, wherein said vesicant comprises a severe vesicant.

6. The formulation according to Claim 1, wherein said vesicant comprises a severe vesicant selected from the group comprising doxorubicin, vincristine, and vinorelbine.

7. The formulation according to Claim 1, wherein said neoplasm is a pulmonary neoplasm, a neoplasm of the head and neck, or other systemic neoplasm.

8. The formulation according to Claim 1, wherein said drug is in the form of a liquid, a powder, a liquid aerosol, or a powdered aerosol.

9. The formulation according to Claim 1, wherein said drug comprises tubulin inhibitors.

10. The formulation according to Claim 1, wherein said drug comprises alkylating agents.

11. The formulation according to Claim 1, wherein said drug comprises an anthracycline.

12. The formulation according to Claim 11, wherein said anthracycline is selected from the group consisting of epirubicin, daunorubicin, methoxymorpholinodoxorubicin, cyanomorpholinyl doxorubicin, doxorubicin, and idarubicin.

13. The formulation according to Claim 12, wherein when doxorubicin is selected said effective amount of said drug for animals is about 2 to 90 mg/m^2 and the human dose is about 3 to 130 mg/m^2, wherein both doses are based on body surface area.

14. The formulation according to Claim 1, wherein said drug is a vinca alkaloid.

15. The formulation according to Claim 14, wherein said vinca alkaloid is selected from the group consisting of vincristine, vinorelbine, vinorelbine, vindesine, and vinblastine.

16. The formulation according to Claim 15, wherein when vincristine is selected the animal dose is about 0.06 to 2 mg/m^2 and the human dose is

about 0.1 to 3 mg/m^2; and when vinorelbine is selected animal dose is about 1.3 to about 60 mg/m^2 and the human dose is about 2 to 90 mg/m^2, wherein all doses are based on body surface area.

17. The formulation according to Claim 1, wherein said drug is a vesicant selected from the group consisting of mechlorethamine, mithramycin, and dactinomycin.

18. The formulation according to Claim 1, wherein said drug is bisantrene.

19. The formulation according to Claim 1, wherein said drug is amsacrine.

20. The formulation according to Claim 1, wherein said drug is a taxane.

21. The formulation according to Claim 1, wherein said drug is paclitaxel.

22. The formulation according to Claim 21, wherein the animal dose is 6 to 90 mg/m^2, and the human dose is 10 to 400 mg/m^2, wherein both doses are based on body surface area.

23. A formulation for treating a patient having a neoplasm by inhalation comprising:

(1) a safe and effective amount of a non-encapsulated antineoplastic drug having a molecular weight above 350, that does not exhibit substantial pulmonary toxicity; and

(2) an effective amount of a pharmaceutically acceptable carrier.

24. The formulation according to Claim 23, wherein said neoplasm is a pulmonary neoplasm, a neoplasm of the head and neck, or a systemic neoplasm.

25. The formulation according to Claim 23, wherein said drug is in the form of a liquid, a powder, a liquid aerosol, or a powdered aerosol.

26. The formulation according to Claim 23, wherein said drug has a protein binding affinity of 25% or more.

27. The formulation according to Claim 26, wherein said drug has a protein binding affinity of 50% or more.

28. The formulation according to Claim 23, wherein said drug has a molecular weight above 400.

29. A formulation for treating a patient for a neoplasm by inhalation comprising: a safe and effective amount of a taxane in an effective amount of vehicle comprising polyethyleneglycol (PEG) and an alcohol.

30. The formulation according to Claim 29, further comprising an acid, said acid present in amount effective to stabilize said taxane.

31. The formulation according to Claim 29, wherein said alcohol is ethanol.

32. The formulation according to Claim 29, wherein said acid is an organic acid.

33. The formulation according to Claim 29, wherein said acid is citric acid.

34. The formulation according to Claim 29, wherein said taxane comprises paclitaxel.

35. The formulation according to Claim 34, comprising about 8% to 40% polyethyleneglycol, about 90% to 60% alcohol, and about 0.01% to 2% acid.

36. The formulation according to Claim 35 wherein said safe and effective amount provides an animal dose of about 6 to about 90 mg/m^2 and a human dose of about 10 to 400 mg/m^2, wherein said dose is based on body surface area.

37. A formulation for treating a patient for a neoplasm by inhalation comprising: a safe and effective amount of a drug selected from the group consisting of carmustine, dacarbazine, melphalan, mercaptopurine, mitoxantrone, esorubicin, teniposide, aclacinomycin, plicamycin, streptozocin, and menogaril; and

a safe and effective amount of a pharmaceutically effective carrier, wherein said drugs do not exhibit substantial pulmonary toxicity.

38. A formulation for treating a patient for a neoplasm by inhalation comprising: a safe and effective amount of a drug selected from the group consisting of estramustine phosphate, geldanamycin, bryostatin, suramin, carboxyamido-triazoles; onconase, and SU101 and its active metabolite SU20; and

a safe and effective amount of a pharmaceutically effective carrier, wherein said drugs do not exhibit substantial pulmonary toxicity.

39. A formulation for treating a patient for a neoplasm by inhalation comprising: a safe and effective amount of etoposide and a DMA carrier.

40. The formulation according to Claim 39, wherein said formulation provides an animal dose of about 4.6 to 200 mg/m^2 and a human dose of about 7 to 300 mg/m^2, wherein said doses are base on body surface area.

41. A formulation for treating a patient for a neoplasm by inhalation comprising: a safe and effective amount of a microsuspension of 9-aminocamptothecin in an aqueous carrier.

42. The formulation according to Claim 39, wherein said formulation provides an animal dose of about 2.6 to 10 mg/m^2 and a human dose of about 0.04 to 15 mg/m^2, wherein said doses are base on body surface area.

43. A formulation for treating a patient having a neoplasm comprising: administering to said patient by inhalation,

(1) an effective amount of a highly toxic antineoplastic drug; and

(2) an effective amount of a chemoprotectant, wherein said chemoprotectant reduces or eliminates toxic effects in said patient that are a result of administering said highly toxic antineoplastic drug.

44. The formulation according to Claim 43, wherein said chemoprotectant reduces or eliminates systemic toxicity in said patient.

45. The formulation according to Claim 43, wherein said chemoprotectant reduces or eliminates respiratory tract toxicity in said patient.

46. The formulation according to Claim 43, wherein said chemoprotectant comprises dexrazoxane (ICRF-187), mesna (ORG-2766), ethiofos (WR2721), or a mixture thereof.

47. The formulation according to Claim 43, wherein said chemoprotectant is administered before, after, or during said administration of said antineoplastic drug.

48. The formulation according to Claim 43, wherein said antineoplastic drug comprises a nonvesicant.

49. The formulation according to Claim 43, wherein said antineoplastic drug comprises a moderate vesicant.

50. The formulation according to Claim 43, wherein said antineoplastic drug comprises a severe vesicant.

51. The formulation according to Claim 43, wherein said antineoplastic drug comprises bleomycin.

52. The formulation according to Claim 43, wherein said antineoplastic drug comprises doxorubicin.

53. The formulation according to Claim 43, wherein said antineoplastic drug comprises mitomycin-C.

54. A method for treating a patient having a neoplasm comprising: administering to said patient by inhalation,

(1) an effective amount of a highly toxic antineoplastic drug; and

(2) an effective amount of a chemoprotectant, wherein said chemoprotectant reduces or eliminates toxic effects in said patient that are a result of administering said highly toxic antineoplastic drug.

55. The method according to Claim 54, wherein said chemoprotectant reduces or eliminates systemic toxicity in said patient.

56. The method according to Claim 54, wherein said chemoprotectant reduces or eliminates respiratory tract toxicity in said patient.

57. The method according to Claim 54, wherein said chemoprotectant comprises dexrazoxane (ICRF-187), mesna (ORG-2766), ethiofos (WR2721), or a mixture thereof.

58. The method according to Claim 54, wherein said chemoprotectant is administered before, after, or during said administration of said antineoplastic drug.

59. The method according to Claim 54, wherein said antineoplastic drug comprises a nonvesicant.

60. The method according to Claim 54, wherein said antineoplastic drug comprises a moderate vesicant.

61. The method according to Claim 54, wherein said antineoplastic drug comprises a severe vesicant.

62. The method according to Claim 54, wherein said antineoplastic drug comprises bleomycin.

63. The method according to Claim 54, wherein said antineoplastic drug comprises doxorubicin.

64. The method according to Claim 54, wherein said antineoplastic drug comprises mitomycin-C.

65. A method for treating a patient having a neoplasm comprising:
administering a pharmaceutically effective amount of a non-encapsulated antineoplastic drug to said patient by inhalation, said drug selected from the group consisting of antineoplastic drugs wherein
when 0.2 ml of said drug is injected intradermally to rats, at the clinical concentration for IV use in humans:

(a) a lesion results which is greater than 20 mm^2 in area fourteen days after said intradermal injection; and

(b) at least 50% of the tested rats have these lesions.

66. The method according to Claim 65, wherein when said drug is doxorubicin or vinblastine sulfate, said drug is inhaled in the absence of perfluorocarbon.

67. The method according to Claim 65, wherein said neoplasm is a pulmonary neoplasm, a neoplasm of the head and neck, or other systemic neoplasm.

68. The method according to Claim 65, wherein said drug is inhaled as a liquid aerosol or as a powdered aerosol.

69. The method according to Claim 65, wherein said patient is a mammal.

70. The method according to Claim 65, wherein said patient is a human.

71. The method according to Claim 65, wherein said drug is an anthracycline selected from the group consisting of doxorubicin, daunorubicin, methoxymorpholinodoxorubicin, epirubicin, cyanomorpholinyl doxorubicin, and idarubicin.

72. The method according to Claim 65, wherein said drug is a vinca alkaloid.

73. The method according to Claim 65, wherein said drug is selected from the group consisting of vincristine, vinorelbine, vindesine, and vinblastine.

74. The method according to Claim 65, wherein said drug is selected from the group consisting of mechlorethamine, mithramycin and dactinomycin.

75. The method according to Claim 65, wherein said drug comprises bisantrene.

76. The method according to Claim 65, wherein said drug comprises amsacrine.

77. The method according to Claim 65, wherein said drug comprises a taxane.

78. The method according to Claim 77, wherein said taxane comprises doxitaxel.

79. The method according to Claim 77, wherein said drug comprises paclitaxel.

80. A method for treating a patient having a neoplasm comprising: administering an effective amount of a highly toxic non-encapsulated antineoplastic drug to a patient by inhalation, wherein the molecular weight of said drug is above 350, and said drug has no substantial pulmonary toxicity.

81. The method according to Claim 80, wherein said neoplasm is a pulmonary neoplasm, a neoplasm of the head and neck, or a systemic neoplasm.

82. The method according to Claim 80, wherein said drug is inhaled as a liquid aerosol or as a powdered aerosol.

83. The method according to Claim 80, wherein said drug has a protein binding affinity of 25% or more.

84. The method according to Claim 83, wherein said drug has a protein binding affinity of 50% or more.

85. The method according to Claim 80, wherein said drug is selected from the group comprising doxorubicin, epirubicin, daunorubicin, methoxymorpholinodoxorubicin, cyanomorpholinyl doxorubicin, and idarubicin.

86. The method according to Claim 80, wherein said drug is a vinca alkaloid administered without the presence of a perfluorocarbon.

87. The method according to Claim 80, wherein said drug is selected from the group consisting of vincristine, vinorelbine, vindesine, and vinblastine.

88. The method according to Claim 80, wherein said drug is mechlorethamine, mithramycin, or dactinomycin.

89. The method according to Claim 80, wherein said drug is bisantrene or amsacrine.

90. The method according to Claim 80, wherein said drug is doxytaxel or paclitaxel.

91. The method according to Claim 80, wherein said patient is a mammal.

92. The method according to Claim 80, wherein said patient is a human.

93. A method for treating a patient for a neoplasm comprising:
administering an effective amount of an antineoplastic drug to said patient by inhalation; and
administering a pharmaceutically effective amount of the same and/or different antineoplastic drug to said patient parenterally.

94. The method according to Claim 93, wherein said patient also is treated by radiotherapy.

95. The method according to Claim 93, wherein said patient is also treated with immunotherapy.

96. The method according to Claim 93, wherein said patient is also treated with gene therapy.

97. The method according to Claim 93, wherein said patient is also administered chemoprotective drugs.

98. The method according to Claim 93 wherein said patient is also administered chemopreventive drugs.

99. A method for treating a patient for a neoplasm comprising:
administering an effective amount of an antineoplastic drug to said patient by inhalation; and
administering an effective amount of the same and/or different antineoplastic drug to said patient by isolated organ perfusion.

100. The method according to Claim 99, wherein said patient is a mammal.

101. The method according to Claim 99, wherein said patient is a human.

102. The method according to Claim 99, wherein said patient is also treated by radiotherapy.

103. The method according to Claim 99, wherein said patient is also treated by immunotherapy.

104. The method according to Claim 99, wherein said patient is also treated by gene therapy.

105. The method according to Claim 99, wherein said patient is also administered chemoprotective drugs.

106. The method according to Claim 99, wherein said patient is also administered chemopreventive drugs.

107. A method for treating a patient for a pulmonary neoplasm comprising:

(1) selecting one or more antineoplastic drugs efficacious in treating said neoplasm and having a residence time in the pulmonary mucosa sufficient to be efficacious in the treatment of said pulmonary neoplasm; and

(2) administering said drug(s) to said patient by inhalation in a non-encapsulated form.

108. The method according to Claim 107, wherein when 0.2 ml of said or at least one of said drugs is injected intradermally to rats, at the clinical concentration for parenteral use in humans:

A. a lesion results which is greater than 20 mm^2 in area fourteen days after said intradermal injection; and

B. at least 50% of the tested rats have these lesions.

109. The method according to Claim 108, wherein said formulation results in a lesion which is greater than about 10 mm^2 in area 30 days after said intradermal injection; and at least about 50% of the tested rats have these longer lasting lesions.

110. The method according to Claim 107, wherein the molecular weight of at least one of said selected drugs is above 350.

111. The method according to Claim 107, wherein said patient is a mammal.

112. The method according to Claim 107, wherein said patient is a human.

113. A method of use, comprising the administration of one or more non-encapsulated highly toxic anticancer drugs to a mammal by inhalation, wherein at least one of said drugs comprises a severe vesicant.

114. An apparatus for treating a patient for a neoplasm by inhalation comprising:

in combination a nebulizer and

a formulation for treating a neoplasm comprising:

(1) a non-encapsulated anticancer drug, and

(2) a pharmaceutically acceptable carrier; wherein when 0.2 ml of said formulation is injected intradermally to rats, at the clinical concentration for parenteral use in humans:

(a) a lesion results which is greater than about 20 mm^2 in area fourteen days after said intradermal injection; and

(b) at least 50% of the tested rats have these lesions.

115. The apparatus according to Claim 114, wherein said formulation results in a lesion which is greater than about 10 mm^2 in area 30 days after said intradermal injection; and at least about 50% of the tested rats have these longer lasting lesions.

116. The apparatus according to Claim 114, wherein said formulation further comprises an anthracycline.

117. The apparatus according to Claim 116, wherein said anthracycline is selected from the group consisting of epirubicin, daunorubicin, methoxymorpholinodoxorubicin, cyanomorpholinyl doxorubicin, doxorubicin, and idarubicin.

118. The apparatus according to Claim 114, wherein said formulation further comprises a vinca alkaloid.

119. The apparatus according to Claim 118, wherein said vinca alkaloid is selected from the group consisting of vincristine, vinorelbine, vinorelbine, vindesine, and vinblastine.

120. The apparatus according to Claim 114, wherein said formulation comprises a vesicant selected from the group consisting of mechlorethamine, mithramycin, and dactinomycin.

121. The apparatus according to Claim 114, wherein said formulation further comprises bisantrene or amsacrine.

122. The apparatus according to Claim 114, wherein said formulation further comprises a taxane.

123. The formulation according to Claim 122, wherein said taxane is paclitaxel or doxytaxel.

124. An inhalation mask for administering aerosols to an patient comprising:
a. means for enclosing the mouth and nose of said patient, having an open end and a closed end, said open end adapted for placing over the mouth and nose of said patient;
b. upper and lower holes in said closed end adapted for insertion of a nose outlet tube and a mouth inhalation tube;
c. said nose outlet tube attached to said upper hole, adapted to accept exhaled breath from the nose of said patient;
d. a one way valve in said nose tube adapted to allow exhalation but not inhalation;
e. said mouth inhalation tube having an outer and an inner end, partially inserted through said lower hole, said inner end continuing to end at the rear of said patients mouth, said inhalation tube end cut at an angle so that the lower portion extends further into said patients mouth than the upper portion and adapted to fit the curvature of the rear of said patients mouth; and
f. a y-adapter attached to the outer end of said mouth inhalation tube.

125. The mask according to Claim 124, further comprising a moderate vesicant present in said inhalation tube.

126. The mask according to Claim 124, further comprising a severe vesicant present in said inhalation tube.

127. Any and all novel features or combination of features, disclosed in the specification of this application.